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<110> KOISHIHARA, YASUO <120> INHIBITOR OF LYMPHOCYTE ACTIVATION <130> 053466/0295 <140> 09/760,723 <141> 2001-01-17 <150> 09/367,833 <151> 1998-08-25 <150> PCT/JP98/00831 <151> 1998-02-27 RECEIVED <160> 8 MAY 3 1 2001 <170> PatentIn Ver. 2.1 TECH CENTER 1600/2900 <210> 1 <211> 1016 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (23)..(562) <223> Nucleotide sequence of DNA coding for HM1.24 antigen <400> 1 gaatteggea egagggatet gg atg gea tet aet teg tat gae tat tge aga Met Ala Ser Thr Ser Tyr Asp Tyr Cys Arg 100 gtg ccc atg gaa gac ggg gat aag cgc tgt aag ctt ctg ctg ggg ata Val Pro Met Glu Asp Gly Asp Lys Arg Cys Lys Leu Leu Gly Ile gga att ctg gtg ctc ctg atc atc gtg att ctg ggg gtg ccc ttg att 148 Gly Ile Leu Val Leu Leu Ile Ile Val Ile Leu Gly Val Pro Leu Ile atc ttc acc atc aag gcc aac agc gag gcc tgc cgg gac ggc ctt cgg 196 Ile Phe Thr Ile Lys Ala Asn Ser Glu Ala Cys Arg Asp Gly Leu Arg 45 gca gtg atg gag tgt cgc aat gtc acc cat ctc ctg caa caa gag ctg 244 Ala Val Met Glu Cys Arg Asn Val Thr His Leu Leu Gln Gln Glu Leu 60 292 acc gag gcc cag aag ggc ttt cag gat gtg gag gcc cag gcc gcc acc Thr Glu Ala Gln Lys Gly Phe Gln Asp Val Glu Ala Gln Ala Ala Thr

85

80

75

tgc aac cac act gtg atg gcc cta atg gct tcc ctg gat gca gag aag Cys Asn His Thr Val Met Ala Leu Met Ala Ser Leu Asp Ala Glu Lys 95 100 gcc caa gga caa aag aaa gtg gag gag ctt gag gga gag atc act aca 388 Ala Gln Gly Gln Lys Lys Val Glu Glu Leu Glu Gly Glu Ile Thr Thr 110 115 tta aac cat aag ctt cag gac gcg tct gca gag gtg gag cga ctg aga 436 Leu Asn His Lys Leu Gln Asp Ala Ser Ala Glu Val Glu Arg Leu Arg 125 130 135 aga gaa aac cag gto tta ago gtg aga ato gog gao aag aag tao tao 484 Arg Glu Asn Gln Val Leu Ser Val Arg Ile Ala Asp Lys Lys Tyr Tyr 140 145 ece age tee cag gae tee age tee get geg geg eee cag etg etg att 532 Pro Ser Ser Gln Asp Ser Ser Ser Ala Ala Pro Gln Leu Leu Ile 155 160 165 170 gtg ctg ctg ggc ctc agc gct ctg ctg cag tgagatccca ggaagctggc 582 Val Leu Leu Gly Leu Ser Ala Leu Leu Gln 175 180 acatettgga aggteegtee tgeteggett ttegettgaa catteeettg ateteateag 642 ttctgagcgg gtcatggggc aacacggtta gcggggagag cacggggtag ccggagaagg 702 gcctctggag caggtctgga ggggccatgg ggcagtcctg ggtgtgggga cacagtcggg 762 ttgacccagg gctgtctccc tccagagcct ccctccggac aatgagtccc ccctcttgtc 822 teccaecetg agattgggea tggggtgegg tgtgggggge atgtgetgee tgttgttatg 882 ggtttttttt gcgggggggg ttgctttttt ctggggtctt tgagctccaa aaaaataaac 942 ttcgggcggc cgcc 1016

<210> 2

<211> 379

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: DNA encoding L chain V region version of a humanized anti-HM1.24 antibody

<220>

<221> CDS

<222> (1)..(378)

<220>

<221> sig_peptide

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<222> (1)..(57)
<220>
<221> mat peptide
<222> (58) .. (378)
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atg gga tgg agc tgt atc atc ctc tcc ttg gta gca aca gct aca ggt
Met Gly Trp Ser Cys Ile Ile Leu Ser Leu Val Ala Thr Ala Thr Gly
                -15
gtc cac tcc gac atc cag atg acc cag agc cca agc agc ctg agc gcc
                                                                   96
Val His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
age gtg ggt gac aga gtg ace ate ace tgt aag get agt cag gat gtg
                                                                   144
Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val
                         20
aat act get gta gee tgg tae eag eag aag eea gga aag get eea aag
                                                                   192
Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
                     35
                                         40
ctq ctq atc tac tcq qca tcc aac cgg tac act ggt gtg cca agc aga
                                                                   240
Leu Leu Ile Tyr Ser Ala Ser Asn Arg Tyr Thr Gly Val Pro Ser Arg
                                     55
ttc agc ggt agc ggt acc gac ttc acc ttc acc atc agc agc
                                                                   288
Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser
ctc cag cca gag gac atc gct acc tac tgc cag caa cat tat agt
Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser
                             85
         80
act cca ttc acg ttc ggc caa ggg acc aag gtg gaa atc aaa c
                                                                   379
Thr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
                        100
                                             105
<210> 3
<211> 418
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: DNA encoding H
      chain V region version r of humanized anti-HM1.24
      antibody
<220>
<221> CDS
<222> (1)..(417)
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<221> sig_peptide
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<220>
<221> mat_peptide
<222> (58)..(417)
<400> 3
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Met Asp Trp Thr Trp Arg Val Phe Phe Leu Leu Ala Val Ala Pro Gly
gct cac tcc cag gtg cag ctg gtg cag tct ggg gct gag gtg aag aag
                                                                   96
Ala His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
cct ggg gcc tca gtg aag gtt tcc tgc aag gca tct gga tac acc ttc
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
act ccc tac tgg atg cag tgg gtg cga cag gcc cct gga caa ggg ctt
                                                                   192
Thr Pro Tyr Trp Met Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
gag tgg atg gga tct att ttt cct gga gat ggt gat act agg tac agt
                                                                   240
Glu Trp Met Gly Ser Ile Phe Pro Gly Asp Gly Asp Thr Arg Tyr Ser
cag aag ttc aag ggc aga gtc acc atg acc gca gac aag tcc acg agc
                                                                   288
Gln Lys Phe Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser
                                 70
aca gcc tac atg gag ctg agc ctg aga tct gag gac acg gcc gtg
Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
tat tac tgt gcg aga gga tta cga cga ggg ggg tac tac ttt gac tac
Tyr Tyr Cys Ala Arg Gly Leu Arg Arg Gly Gly Tyr Tyr Phe Asp Tyr
                        100
                                                                   418
tgg ggg caa ggg acc acg gtc acc gtc tcc tca g
Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
110
                    115
<210> 4
<211> 418
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: DNA encoding H
      chain V region version s of anti-HM1.24 antibody
<220>
<221> CDS
<222> (1)..(417)
<220>
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b

<221> sig peptide

<222> (1)..(57) <220> <221> mat_peptide <222> (58)..(417) <400> 4 atg gac tgg acc tgg agg gtc ttc ttc ttg ctg gct gta gct cca ggt 48 Met Asp Trp Thr Trp Arg Val Phe Phe Leu Leu Ala Val Ala Pro Gly -15 gct cac tcc cag gtg cag ctg gtg cag tct ggg gct gag gtg aag aag 96 Ala His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys cct ggg gcc tca gtg aag gtt tcc tgc aag gca tct gga tac acc ttc 144 Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe 15 2.0 act ecc tac tgg atg cag tgg gtg ega cag gee eet gga caa ggg ett 192 Thr Pro Tyr Trp Met Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu 40 gag tgg atg gga tct att ttt cct gga gat ggt gat act agg tac agt 240 Glu Trp Met Gly Ser Ile Phe Pro Gly Asp Gly Asp Thr Arg Tyr Ser 50 5.5 cag aag ttc aag ggc aga gtc acc atc acc gca gac aag tcc acg agc 288 Gln Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser 70 aca gcc tac atg gag ctg agc agc ctg aga tct gag gac acg gcc gtg Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val tat tac tgt gcg aga gga tta cga cga ggg ggg tac tac ttt gac tac Tyr Tyr Cys Ala Arg Gly Leu Arg Arg Gly Gly Tyr Tyr Phe Asp Tyr 100 418 tgg ggg caa ggg acc acg gtc acc gtc tcc tca g Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 110 115 120 <210> 5 <211> 180 <212> PRT <213> Homo sapiens <220> <223> Amino acid sequence of HM1.24 antigen <400> 5 Met Ala Ser Thr Ser Tyr Asp Tyr Cys Arg Val Pro Met Glu Asp Gly Asp Lys Arg Cys Lys Leu Leu Gly Ile Gly Ile Leu Val Leu Leu

b

20

Ile Ile Val Ile Leu Gly Val Pro Leu Ile Ile Phe Thr Ile Lys Ala 35 40 45

Asn Ser Glu Ala Cys Arg Asp Gly Leu Arg Ala Val Met Glu Cys Arg 50 $\,$ 55 $\,$ 60

Asn Val Thr His Leu Leu Gln Gln Glu Leu Thr Glu Ala Gln Lys Gly 65 70 75 80

Phe Gln Asp Val Glu Ala Gln Ala Ala Thr Cys Asn His Thr Val Met 85 90 95

Ala Leu Met Ala Ser Leu Asp Ala Glu Lys Ala Gln Gly Gln Lys Lys
100 105 110

Val Glu Glu Leu Glu Gly Glu Ile Thr Thr Leu Asn His Lys Leu Gln
115 120 125

Asp Ala Ser Ala Glu Val Glu Arg Leu Arg Arg Glu Asn Gln Val Leu 130 135 140

Ser Val Arg Ile Ala Asp Lys Lys Tyr Tyr Pro Ser Ser Gln Asp Ser 145 150 155 160

Ser Ser Ala Ala Pro Gln Leu Leu Ile Val Leu Leu Gly Leu Ser 165 170 175

Ala Leu Leu Gln 180

<210> 6

<211> 126

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Amino acid sequence
 of L chain V region version a of humanized anti-HM1.24
 antibody

<400> 6

Met Gly Trp Ser Cys Ile Ile Leu Ser Leu Val Ala Thr Ala Thr Gly
-15 -10 -5

Val His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
-1 1 5 10

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val 15 20 25

Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys 30 35 40 45

Leu Leu Ile Tyr Ser Ala Ser Asn Arg Tyr Thr Gly Val Pro Ser Arg

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser
65 70 75

Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln His Tyr Ser 80 85 90

Thr Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys 95 100 105

<210> 7

<211> 139

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Amino acid sequence of H chain V region version r of humanized anti-HM1.24 antibody

<400> 7

Met Asp Trp Thr Trp Arg Val Phe Phe Leu Leu Ala Val Ala Pro Gly
-15 -10 -5

Ala His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
-1 1 5 10

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe 15 20 25

Thr Pro Tyr Trp Met Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu 30 35 40 45

Glu Trp Met Gly Ser Ile Phe Pro Gly Asp Gly Asp Thr Arg Tyr Ser 50 55 60

Gln Lys Phe Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser
65 70 75

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val

Tyr Tyr Cys Ala Arg Gly Leu Arg Arg Gly Gly Tyr Tyr Phe Asp Tyr 95 100 105

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 110 125

<210> 8

<211> 139

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Amino acid sequence of H chain V region version s of humanized

82

anti-HM1.24 antibody

<400> 8

Met Asp Trp Thr Trp Arg Val Phe Phe Leu Leu Ala Val Ala Pro Gly
-15 -10 -5

Ala His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
-1 1 5 10

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
15 20 25

Thr Pro Tyr Trp Met Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu 30 45

Glu Trp Met Gly Ser Ile Phe Pro Gly Asp Gly Asp Thr Arg Tyr Ser 50 55 60

Gln Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser 65 70 75

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val $80 \\ 85 \\ 90$

Tyr Tyr Cys Ala Arg Gly Leu Arg Arg Gly Gly Tyr Tyr Phe Asp Tyr 95 100 105

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 110 115 120

